REPORT DOCUMENTATION PAGE

Form Approved
OMB NO. 0704-0188

Public reporting burden for this collection of information is estimated to average 1 hour per response, including the time for reviewing instructions. searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comment regarding this burden estimates or any other aspect of this collection of information, including suggestions for reducing this burden, to Washington Headquarters Services, Directorate for information Operations and Reports, 1215 Jefferson Davis Highway, Suite 1204, Arlington, VA 22202-4302, and to the Office of Management and Budget, Paperwork Reduction Project (0704-0188), Washington, DC 20503.

1. AGENCY USE ONLY *(Leave blank)*	2. REPORT DATE 16 Aug 99	3. REPORT TYPE AND DATES COVERED Final

4. TITLE AND SUBTITLE
Developing and understanding methods for large-scale nonlinear optimization

5. FUNDING NUMBERS
DAAH04-94-G-0228

6. AUTHOR(S)
Robert B. Schnabel and Richard H. Byrd

7. PERFORMING ORGANIZATION NAMES(S) AND ADDRESS(ES)
University of Colorado at Boulder
Office of Contracts and Grants
Armory 206, Campus Box 19
Boulder, CO 80309

8. PERFORMING ORGANIZATION REPORT NUMBER

9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)
U.S. Army Research Office
P.O. Box 12211
Research Triangle Park, NC 27709-2211

10. SPONSORING / MONITORING AGENCY REPORT NUMBER
ARO 32846.10-MA

11. SUPPLEMENTARY NOTES
The views, opinions and/or findings contained in this report are those of the author(s) and should not be construed as an official Department of the Army position, policy or decision, unless so designated by other documentation.

12a. DISTRIBUTION / AVAILABILITY STATEMENT
Approved for public release; distribution unlimited.

12 b. DISTRIBUTION CODE

19991101 125

13. ABSTRACT *(Maximum 200 words)*

The most important contribution under this grant has been a vast improvement in the ability of large-scale global optimization methods to solve very difficult molecular configuration problems. The improvements are shown both in the size and in the complexity of the problems that can now be solved. At the beginning of this research period, we and others were just beginning to solve molecular cluster problems with up to hundreds of parameters. By the end of the research period, we had progressed from these cluster problems to much more difficult and important protein folding problems with thousands of variables. The most fundamental research advance that contributed to the improvements in our large-scale global optimization algorithms was the development and understanding of new smoothing approaches. Other significant research contributions included: the successful application of our global optimization approach to distance geometry problems; the development of a new primal-dual interior point method for nonlinearly constrained optimization; and the modification and improvement of our widely used modified Cholesky factorization method.

14. SUBJECT TERMS
Nonlinear Optimization   Molecular Chemistry
Global Optimization   Constrained Optimization

15. NUMBER IF PAGES
8

16. PRICE CODE

17. SECURITY CLASSIFICATION OR REPORT UNCLASSIFIED	18. SECURITY CLASSIFICATION OF THIS PAGE UNCLASSIFIED	19. SECURITY CLASSIFICATION OF ABSTRACT UNCLASSIFIED	20. LIMITATION OF ABSTRACT UL

NSN 7540-01-280-5500

Standard Form 298 (Rev. 2-89)
Prescribed by ANSI Std. 239-18
298-102

FINAL REPORT for

ARO Grant DAAH04-94-G-0228
Developing and Understanding Methods for
Large-Scale Nonlinear Optimization
1 July 1994 - 31 March 1998

Principal Investigator: Robert B. Schnabel
Co-Principal Investigator: Richard H. Byrd

1. Statement of the Problem Studied

The area of this research is the numerical solution of nonlinear optimization problems. Optimization problems are one of the main forms of mathematical problems whose computer solution is desired by scientists and engineers. The need to solve such problems arises in a huge variety of computer simulations and data analyses, with examples including optimal design of aircraft and spacecraft for low cost or high efficiency, optimal control of chemical processes, and calculation of the native states of biological molecules. In recent years, as computer power has increased, the feasibility of investigating optimal designs has increased, and along with this the need for improved optimization methods has grown. This requires fundamental research in optimization algorithms, especially for classes of large-scale problems. In addition, much of this computation must utilize the fastest available computers, which increasingly are parallel computers. Thus the development of optimization methods that are well-suited to parallel computers is also a pressing need.

One of the main emphases of this research program in recent years has been the development of global optimization methods for the solution of large molecular configuration problems. Global optimization means finding the lowest minimizer of a nonlinear function that may have numerous local minimizers. The objective of this research is to develop methods that are reliably capable of solving difficult, large nonlinear global optimization problems. Our current work is investigating methods to find the native configurations of proteins and polymers. This is a problem of great importance in science; it includes the well-known protein folding problem as well as the investigation of polymers that are used to make new materials. The resultant optimization problems are very difficult because they have extremely large numbers of local minimizers that have similar function values.

Another main focus of our research is the development of new algorithms for large-scale unconstrained and constrained optimization problems, including limited-memory methods for problems with many thousands of variables, and interior point methods for nonlinearly constrained problems. We are also investigating theoretical convergence issues for optimization algorithms that have practical consequences in how problems are formulated, and new approaches to one of the key numerical linear algebra subproblems that is particular to optimization algorithms.

2. Summary of the Most Important Results

The most important contribution under this grant has been a vast improvement in the ability of large-scale global optimization methods to solve very difficult molecular configuration problems. The improvements are shown both in the size and in the complexity of the problems that can now be solved. At the beginning of this research period, we were just beginning to solve molecular cluster problems with up to hundreds of parameters. By the end of the research period, we had progressed from these cluster problems to much more difficult and important protein folding problems with thousands of variables.

The most fundamental research advance that contributed to the improvements in our large-scale global optimization algorithms was the development and understanding of new smoothing approaches. Smoothing refers to approaches that replace the highly nonlinear objective function by one that retains its coarse grain features but reduce its fine grain variations. The basic objective of smoothing is to first solve an easier computational problem using the smoothed function and then use this to find the solution of the original problem. Smoothing has been applied to global optimization problems from molecular chemistry before, but involved the use of expensive convolution-based approaches that also required ah-hoc approximations to eliminate poles. One main contribution of our research was the introduction a simple, cheap, analytic method of smoothing molecular chemistry objective functions, and demonstration that it performs as well as previous, expensive smoothing approaches. Careful experiments showed that our simpler and cheaper function was qualitatively very similar in its form and its properties as the functions that result from convolution. A second contribution was been to demonstrate, via experiments, some fundamental limitations of smoothing approaches for global optimization that may not have been recognized previously. In particular, we showed that for a variety of problems, smoothing introduces very significant "order flips", meaning that the order of the smoothed minimizers does not correspond to the order of the nonsmoothed minimizers from which they descend. This research showed that it is not sufficient to combine smoothing with local optimization as had previously been done; rather global optimization techniques must be used at various levels of smoothing.

Based on this understanding, we developed an algorithmic framework that combines smoothing with the PI's stochastic-perturbation global optimization approach for large-scale global optimization. We also made significant refinements to the stochastic-perturbation approach to permit it to apply to protein problems as opposed to molecular clusters. These particularly included the development of new heuristics to select the parameters which are used in the crucial small scale global optimization phase of our method, as well as entirely new methods to generate initial structures for our method. The combination of the two approaches, the modified stochastic-perturbation method and smoothing, produced very promising results. Most importantly, we were able to find optimal configurations of the protein polyalanine for 20, 30, 40 and 58 amino acids (with approximately 30 variables per amino acid). In the first three cases, the optimal structure is alpha-helical, and could be found by our algorithm with or without smoothing, but was found far more readily with smoothing for the large protein. In the last case, the optimal solution consists of two alpha-helical segments connected with a turn in the rough overall shape of the character alpha. While chemists had shown simply by generating configurations that this was a lower energy structure than a straight alpha helix, we believe that ours is the first work to find this shape via optimization techniques. This shows the promise of our approach for finding the complex shapes of more complicated proteins. Smoothing proved crucial in both the efficiency and the quality of our work on this larger protein. Our ongoing research is now considering more difficult proteins and further algorithmic improvements.

As part of this research, we began utilizing "biasing" techniques in our generation of initial structures. This work, conducted in conjunction with the group of Teresa-Head Gordon of Lawrence Berkeley Laboratory, is based upon the antlion approach that she developed with F. Stillinger of Bell Labs. From an optimization viewpoint, it uses penalty terms to reward secondary structure that has been predicted by techniques such as neural nets. Experiments with polyalanine showed that biasing has the potential to greatly improve our initial structures, and that it should be an important part of techniques for more complex proteins.

A related advance was the application of our global optimization methodology to a quite different class of problems, distance geometry problems, that also arise in molecular chemistry. Distance geometry problems also are global optimization problems that arise from trying to find the configuration that comes closest to matching a set of approximate pairwise distances between some subset of the pairs of atoms in a molecule. Our stochastic perturbation approach was significantly more successful than previously tried optimization approaches in solving test problems with up to 2000 variables. This research demonstrates the versatility of our global optimization approach.

Earlier in the research period we applied our stochastic-perturbation global optimization approach to molecular cluster problems with excellent results. We completed the testing of our methods on two well-known molecular cluster problems, Lennard-Jones clusters and water. On the much-studied Lennard-Jones problems, our method produced better results than any known general or special purpose method, for problems with up to 76 atoms (228 parameters). This included finding the best known minimizers for all of these problems, a new lower minimizer for the 75 atom problem, and recently discovered lower minimizers for the 66 and 72 atom problems. The method also found far lower energy configurations for clusters of water molecules with up to 288 parameters than a previous method developed by chemists.

In our research on limited memory methods for large scale problems, we developed high quality software for our new approach for solving large nonlinear optimization problems subject to simple bounds on the variables. This software is intended for problems in which information on the Hessian matrix is difficult to obtain, or for large dense problems.

Our research in large scale constrained optimization concentrated on the development of interior point approaches for nonlinearly constrained problems. This work has resulted in a new primal method with strong global convergence properties. Additionally, experiments with primal and primal-dual versions of this method have demonstrated promising computational performance on large scale problems. Ongoing research appears to be establishing this approach as one of the leading ones for large scale constrained optimization.

In the convergence analysis of singular constrained optimization problems, we developed a new set of optimality conditions for singular equality constrained optimization problems. These appear to be the first conditions that deal effectively with the important practical case where the Jacobian matrix of the constraints is singular at the solution and the Lagrange multipliers are unbounded. We can show that our new optimality condition is a necessary condition for singular constrained minimizers satisfying rather general conditions, as well as being satisfied for a broad set of problems.

Another significant contribution has been an improvement to our modified Cholesky factorization algorithm. The modified Cholesky factorization is an essential element of many unconstrained and constrained optimization approaches. Our new algorithm, introduced several years ago, has become widely

used, but recently some cases had arisen where its performance was not good, especially in interior point approaches to constrained optimization. A fairly simple modification to the factorization has enabled it to handle all known problematic cases excellently, while still retaining its previous good computational and theoretical properties.

Finally, we completed research on several topics in tensor methods, for large scale and constrained optimization. We also completed and released software for using tensor methods for solving systems on nonlinear equations and nonlinear least squares problems. This software has been used extensively and appears to be effective in enabling users to solve some problems that they couldn't solve before, or to solve problems more efficiently.

3. List of All Publications and Technical Reports

(1)   A. Bouaricha and R. Schnabel, "TENSOLVE: A software package for solving systems of nonlinear equations and nonlinear least squares problems using tensor methods", *ACM Transactions on Mathematical Software* 23, 1997, pp. 174-195.

(2)   A. Bouaricha and R. Schnabel, "Tensor methods for large sparse systems of nonlinear equations", *Mathematical Programming* 82, 1998, pp. 377-400.

(3)   A. Bouaricha and R. Schnabel, "Tensor methods for large sparse nonlinear least squares problems", to appear in *SIAM Journal on Scientific Computing.*

(4)   R. Byrd, E. Eskow, A. van der Hoek, R. Schnabel, C.-S. Shao, and Z. Zou, "Global optimization methods for protein folding problems", *Global Minimization of Nonconvex Energy Functions: Molecular Conformation and Protein Folding,* P. Pardalos, D. Shalloway, and G. Xue, eds., American Mathematical Society, 1995, pp. 29-39.

(5)   R. Byrd, E. Eskow, B. Oldenkamp, R. Schnabel and A. van der Hoek, "A parallel global optimization method for solving molecular cluster and polymer conformation problems", Proceedings of the Seventh SIAM Conference on Parallel Processing for Scientific Computing, SIAM, 1995, pp. 72-77.

(6)   R. Byrd, E. Eskow and R. Schnabel, "A new large-scale global optimization method and its application to Lennard-Jones problems", University of Colorado Technical Report CU-CS-630-92 (revised and resubmitted for publication).

(7)   R. Byrd, D. Feng and R. Schnabel, "On optimality conditions for singular constrained optimization", submitted for publication.

(8)   R. Byrd, J. Gilbert and J. Nocedal, "A trust region method based on interior point techniques for nonlinear programming", Technical Report, Department of Computer Science, University of Colorado, Boulder, submitted for publication.

(9)   R. Byrd, M. Hribar and J. Nocedal, "An interior point algorithm for large scale nonlinear programming", to appear in *SIAM Journal on Optimization.*

(10)   R. Byrd, H. Khalfan and R. Schnabel, "Analysis of a symmetric rank-one trust region method", *SIAM Journal on Optimization* 6, 1996, pp. 1025-1039.

(11)   R. Byrd, G. Liu and J. Nocedal, "On the local behavior of an interior point method for nonlinear programming", in *Numerical Analysis 1997, Proceedings of the 17th Dundee Biennial Conference,* D.F. Griffiths, D.J. Higham and G.A. Watson, eds., Addison Wesley Longman pp. 37-56.

(12)   R. Byrd, J. Nocedal and C. Zhu, "Towards a discrete Newton method with memory for large-scale optimization, in *Nonlinear Optimization and Applications,* G.Di Pillo and F. Giannesi, eds., Plenum.

(13)   R. Byrd and Y. Xie, "Practical update criteria for reduced Hessian successive quadratic programming algorithms," Technical Report CU-CS-753-94, Dept. of Computer Science, Univ. of Colorado, to appear in *SIAM Journal on Optimization.*

(14) R. Byrd and Y. Yuan, "Non-quasi-Newton updates for unconstrained optimization", *Journal of Computational Mathematics 13,* (1995) pp.95-107.

(15) R. Byrd, C. Zhu, P. Lu and J. Nocedal, "L-BFGS-B -- Fortran subroutines for large-scale bound constrained optimization", *Transactions on Mathematical Software 23 (1997) pp.550-560.*

(16) T. Chow, E. Eskow and R. Schnabel, "A software package for unconstrained optimization using tensor methods," *ACM Transactions on Mathematical Software* 20, 1994, pp. 518-530.

(17) D. Feng and R. Schnabel, "Tensor methods for equality constrained optimization", *SIAM Journal on Optimization* 6, 1996, pp. 653-673.

(18) D. Feng and R. Schnabel, "Local convergence analysis of tensor and SQP methods for singular constrained optimization", provisionally accepted for publication in *SIAM Journal on Optimization.*

(19) M. Rosing and R. Schnabel, "Flexible language constructs for large parallel programs", *Scientific Programming* 3, 1994, pp. 169-186.

(20) R. Schnabel, "A view of the limitations, opportunities, and challenges in parallel nonlinear optimization", *Parallel Computing* 21, 1995, pp. 875-905.

(21) R. Schnabel and E. Eskow, "A revised modified Cholesky factorization algorithm", to appear in *SIAM Journal on Optimization,* Sept. 1999.

(22) C.-S. Shao, R. Byrd, E. Eskow and R. Schnabel, "Global optimization for molecular cluster problems using a new smoothing approach", *Large-Scale Optimization with Applications, Part III: Molecular Structure and Optimization",* L. Biegler, T. Coleman, A. Conn and F. Santosa, eds., Springer, 1997, pp. 163-199.

(23) C.-S. Shao, R. Byrd, E. Eskow and R. Schnabel, "Global optimization for molecular clusters using a new smoothing approach", to appear in *Journal of Global Optimization.*

(24) Z. Zou, R. Byrd and R. Schnabel, "A stochastic/perturbation global optimization algorithm for distance geometry problems", *Journal on Global Optimization* 11, 1997, pp. 91-105.

4. List of Participating Scientific Personnel

Xuehua Lu, Ph.D. 1996

Aqil Azmi, Ph. D 1998

Joe McCormick. M.S. 1997

Anna Szczyrba. M.S. 1998

Ciyou Zhu

5. Report of Inventions